

WHAT IS CLAIMED IS:

1. A method for treating a thrombotic disease in a mammal, said method comprising:

administering to said mammal a therapeutically effective amount of a
5 pharmaceutical composition comprising a viral vector,
wherein said viral vector comprises a nucleotide sequence encoding human thrombomodulin or its variant, and wherein said human thrombomodulin has an amino acid sequence recited in SEQ ID NO:2.

2. The method of Claim 1, wherein said pharmaceutical composition
10 further comprises a pharmaceutically acceptable carrier.

3. The method of Claim 1, wherein said viral vector is an adenovirus.

4. The method of Claim 3, wherein said adenovirus is a gutless adenovirus.

5. The method of Claim 4, wherein said gutless adenovirus is produced using a shuttle vector comprising the nucleotide sequence recited in SEQ ID NO: 4.

6. The method of Claim 1, wherein said nucleotide sequence encoding
15 human thrombomodulin or its variant is operably linked to a constitutive promoter.

7. The method of Claim 1, wherein said nucleotide sequence encoding human thrombomodulin or its variant is operably linked to a tissue-specific promoter.

8. The method of Claim 1, wherein said nucleotide sequence encoding
20 human thrombomodulin or its variant is under the control of a regulatable expression system.

9. The method of Claim 1, wherein said thrombotic disease is atherosclerotic cardiovascular disease, pulmonary hypertension, acute inflammatory diseases, end-stage renal failure disease, or Alzheimer disease.

5 10. The method of Claim 1, wherein said viral vector is an adeno-associated virus.

11. The method of Claim 1, wherein said viral vector is a retrovirus.

12. The method of Claim 1, wherein said viral vector is a lentivirus.

13. The method of Claim 12, wherein said lentivirus is a human immunodeficiency virus.

10 14. The method of Claim 1, wherein said viral vector is a herpes virus.

15. The method of Claim 1, wherein said pharmaceutical composition is administered to said mammal intravascularly, subcutaneously, or intramuscularly.

16. A method for treating a thrombotic disease in a mammal, said method comprising:

15 administering to said mammal a therapeutically effective amount of a pharmaceutical composition comprising a non-viral vector, wherein said non-viral vector comprises a nucleotide sequence encoding human thrombomodulin or its variant, and wherein said human thrombomodulin has an amino acid sequence recited in SEQ ID NO:2.

20 17. The method of Claim 16, wherein said pharmaceutical composition further comprises a pharmaceutically acceptable carrier.

18. The method of Claim 16, wherein said non-viral vector is a liposome.

19. The method of Claim 16, wherein said non-viral vector is a naked DNA molecule.

20. The method of Claim 16, wherein the nucleotide sequence encoding human thrombomodulin or its variant is operably linked to a constitutive promoter.

21. The method of Claim 16, wherein the nucleotide sequence encoding human thrombomodulin or its variant is operably linked to a tissue-specific promoter.

22. The method of Claim 16, wherein the nucleotide sequence encoding human thrombomodulin or its variant is under the control of a regulatable expression system.

23. The method of Claim 16, wherein said thrombotic disease is atherosclerotic cardiovascular disease, pulmonary hypertension, acute inflammatory diseases, end-stage renal failure disease, or Alzheimer disease.

24. A method for treating a thrombotic disease in a mammal, said method comprising:

administering to said mammal a therapeutically effective amount of thrombomodulin-producing cells,

wherein said thrombomodulin-producing cells are generated by introducing a polynucleotide encoding a human thrombomodulin or its variant into a cultured cell, and wherein said human thrombomodulin has an amino acids sequence recited in SEQ ID NO:2.

25. The method of Claim 24, wherein said culture cell is human umbilical vein endothelium cell (HUVEC).

26. The method of Claim 24, wherein said polynucleotide encoding a human thrombomodulin or its variant is introduced into said cultured cell by a viral vector.

27. The method of Claim 24, wherein said polynucleotide encoding a human thrombomodulin or its variant is introduced into said cultured cell by a non-viral vector.

28. The method of Claim 24, wherein said polynucleotide encoding a
5 human thrombomodulin or its variant is introduced into said cultured cell by calcium phosphate precipitation.

29. The method of Claim 24, wherein said polynucleotide encoding a human thrombomodulin or its variant is introduced into said cultured cell by electroporation.